

SUBSTITUTE SEQUENCE LISTING

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JAN 27 2003
TECH CENTER 1600/2900

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<120> Beta-Secretase Enzyme Compositions and
Methods

<130> 228-US-NEWC1

<140> 09/723,722

<141> 2000-11-28

<150> US 09/501,708

<151> 2000-02-10

<150> 60/119,571

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<150> 60/139,172

<151> 1999-06-15

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Glu	Glu	Pro	Glu	Glu	Pro	Gly	Arg	Arg	Gly	Ser	Phe	Val	Glu	Met	Val	50	55	60	
Asp	Asn	Leu	Arg	Gly	Lys	Ser	Gly	Gln	Gly	Tyr	Tyr	Val	Glu	Met	Thr	65	70	75	80
Val	Gly	Ser	Pro	Pro	Gln	Thr	Leu	Asn	Ile	Leu	Val	Asp	Thr	Gly	Ser	85	90	95	
Ser	Asn	Phe	Ala	Val	Gly	Ala	Ala	Pro	His	Pro	Phe	Leu	His	Arg	Tyr	100	105	110	
Tyr	Gln	Arg	Gln	Leu	Ser	Ser	Thr	Tyr	Arg	Asp	Leu	Arg	Lys	Gly	Val	115	120	125	
Tyr	Val	Pro	Tyr	Thr	Gln	Gly	Lys	Trp	Glu	Gly	Glu	Leu	Gly	Thr	Asp	130	135	140	
Leu	Val	Ser	Ile	Pro	His	Gly	Pro	Asn	Val	Thr	Val	Arg	Ala	Asn	Ile	145	150	155	160
Ala	Ala	Ile	Thr	Glu	Ser	Asp	Lys	Phe	Phe	Ile	Asn	Gly	Ser	Asn	Trp	165	170	175	
Glu	Gly	Ile	Leu	Gly	Leu	Ala	Tyr	Ala	Glu	Ile	Ala	Arg	Pro	Asp	Asp	180	185	190	
Ser	Leu	Glu	Pro	Phe	Phe	Asp	Ser	Leu	Val	Lys	Gln	Thr	His	Val	Pro	195	200	205	
Asn	Leu	Phe	Ser	Leu	Gln	Leu	Cys	Gly	Ala	Gly	Phe	Pro	Leu	Asn	Gln	210	215	220	
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Asp	His	Ser	Leu	Tyr	Thr	Gly	Ser	Leu	Trp	Tyr	Thr	Pro	Ile	Arg	Arg	245	250	255	
Glu	Trp	Tyr	Tyr	Glu	Val	Ile	Ile	Val	Arg	Val	Glu	Ile	Asn	Gly	Gln	260	265	270	
Asp	Leu	Lys	Met	Asp	Cys	Lys	Glu	Tyr	Asn	Tyr	Asp	Lys	Ser	Ile	Val	275	280	285	
Asp	Ser	Gly	Thr	Thr	Asn	Leu	Arg	Leu	Pro	Lys	Lys	Val	Phe	Glu	Ala	290	295	300	
Ala	Val	Lys	Ser	Ile	Lys	Ala	Ala	Ser	Ser	Thr	Glu	Lys	Phe	Pro	Asp	305	310	315	320
Gly	Phe	Trp	Leu	Gly	Gln	Leu	Val	Cys	Trp	Gln	Ala	Gly	Thr	Thr		325	330	335	
Pro	Trp	Asn	Ile	Phe	Pro	Val	Ile	Ser	Leu	Tyr	Leu	Met	Gly	Glu	Val	340	345	350	
Thr	Asn	Gln	Ser	Phe	Arg	Ile	Thr	Ile	Leu	Pro	Gln	Gln	Tyr	Leu	Arg	355	360	365	

Pro Val Glu Asp Val Ala Thr Ser Gln Asp Asp Cys Tyr Lys Phe Ala
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 Ile Ser Gln Ser Ser Thr Gly Thr Val Met Gly Ala Val Ile Met Glu
 385 390 395 400
 Gly Phe Tyr Val Val Phe Asp Arg Ala Arg Lys Arg Ile Gly Phe Ala
 405 410 415
 Val Ser Ala Cys His Val His Asp Glu Phe Arg Thr Ala Ala Val Glu
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 Gly Pro Phe Val Thr Leu Asp Met Glu Asp Cys Gly Tyr Asn Ile Pro
 435 440 445
 Gln Thr Asp Glu Ser Thr Leu Met Thr Ile Ala Tyr Val Met Ala Ala
 450 455 460
 Ile Cys Ala Leu Phe Met Leu Pro Leu Cys Leu Met Val Cys Gln Trp
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 ID NO: 2

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<223> Degenerate oligonucleotide primer

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<210> 31

<211> 27

<212> DNA

<213> Artificial Sequence

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<223> Degenerate oligonucleotide primer

<400> 31

atattctaga gaygargagc cggaaga

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<210> 32

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<210> 33

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 35 40 45
 Thr Gly Ser Ser Asn Phe Ala Val Gly Ala Ala Pro His Pro Phe Leu
 50 55 60
 His Arg Tyr Tyr Gln Arg Gln Leu Ser Ser Thr Tyr Arg Asp Leu Arg
 65 70 75 80
 Lys Gly Val Tyr Val Pro Tyr Thr Gln Gly Lys Trp Glu Gly Glu Leu
 85 90 95
 Gly Thr Asp Leu Val Ser Ile Pro His Gly Pro Asn Val Thr Val Arg
 100 105 110
 Ala Asn Ile Ala Ala Ile Thr Glu Ser Asp Lys Phe Phe Ile Asn Gly
 115 120 125
 Ser Asn Trp Glu Gly Ile Leu Gly Leu Ala Tyr Ala Glu Ile Ala Arg
 130 135 140
 Pro Asp Asp Ser Leu Glu Pro Phe Phe Asp Ser Leu Val Lys Gln Thr
 145 150 155 160
 His Val Pro Asn Leu Phe Ser Leu Gln Leu Cys Gly Ala Gly Phe Pro
 165 170 175
 Leu Asn Gln Ser Glu Val Leu Ala Ser Val Gly Gly Ser Met Ile Ile
 180 185 190
 Gly Gly Ile Asp His Ser Leu Tyr Thr Gly Ser Leu Trp Tyr Thr Pro
 195 200 205
 Ile Arg Arg Glu Trp Tyr Tyr Glu Val Ile Ile Val Arg Val Glu Ile
 210 215 220
 Asn Gly Gln Asp Leu Lys Met Asp Cys Lys Glu Tyr Asn Tyr Asp Lys
 225 230 235 240
 Ser Ile Val Asp Ser Gly Thr Thr Asn Leu Arg Leu Pro Lys Lys Val
 245 250 255
 Phe Glu Ala Ala Val Lys Ser Ile Lys Ala Ala Ser Ser Thr Glu Lys
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 Gly Thr Thr Pro Trp Asn Ile Phe Pro Val Ile Ser Leu Tyr Leu Met
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 Gly Glu Val Thr Asn Gln Ser Phe Arg Ile Thr Ile Leu Pro Gln Gln
 305 310 315 320
 Tyr Leu Arg Pro Val Glu Asp Val Ala Thr Ser Gln Asp Asp Cys Tyr
 325 330 335
 Lys Phe Ala Ile Ser Gln Ser Ser Thr Gly Thr Val Met Gly Ala Val
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 Ile Met Glu Gly Phe Tyr Val Val Phe Asp Arg Ala Arg Lys Arg Ile
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 Gly Phe Ala Val Ser Ala Cys His Val His Asp Glu Phe Arg Thr Ala
 370 375 380
 Ala Val Glu Gly Pro Phe Val Thr Leu Asp Met Glu Asp Cys Gly Tyr
 385 390 395 400
 Asn Ile Pro Gln Thr Asp Glu Ser Thr Leu Met Thr Ile Ala Tyr Val
 405 410 415
 Met Ala Ala Ile Cys Ala Leu Phe Met Leu Pro Leu Cys Leu Met Val
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 <212> DNA
 <213> Homo sapiens

<400> 49
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32

<210> 50
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 <212> PRT
 <213> Homo sapiens

<400> 50
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<210> 51
 <211> 5
 <212> PRT
 <213> Homo sapiens

<400> 51
 Val Asn Leu Asp Ala
 1 5

<210> 52
 <211> 9
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Synthetic oligopeptide substrate

<400> 52

Ser Glu Val Asn Leu Asp Ala Glu Phe
1 5

<210> 53

<211> 30

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic oligopeptide substrate

<400> 53

Ala Asp Arg Gly Leu Thr Thr Arg Pro Gly Ser Gly Leu Thr Asn Ile
1 5 10 15
Lys Thr Glu Glu Ile Ser Glu Val Asn Leu Asp Ala Glu Phe
20 25 30

<210> 54

<211> 5

<212> PRT

<213> Homo sapiens

<220>

<223> Wild type Amyloid Precursor Protein cleavage site
(fragment)

<400> 54

Val Lys Met Asp Ala
1 5

<210> 55

<211> 24

<212> PRT

<213> Homo sapiens

<400> 55

Glu Thr Asp Glu Glu Pro Glu Glu Pro Gly Arg Arg Gly Ser Phe Val
1 5 10 15
Glu Met Val Asp Asn Leu Arg Gly
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<210> 56

<211> 15

<212> PRT

<213> Homo sapiens

<400> 56

Ile Gly Phe Ala Val Ser Ala Cys His Val His Asp Glu Phe Arg
1 5 10 15

<210> 57

<211> 419

<212> PRT

<213> Homo sapiens

<400> 57

Met Ala Gln Ala Leu Pro Trp Leu Leu Leu Trp Met Gly Ala Gly Val
1 5 10 15
Leu Pro Ala His Gly Thr Gln His Gly Ile Arg Leu Pro Leu Arg Ser
20 25 30

Gly Leu Gly Gly Ala Pro Leu Gly Leu Arg Leu Pro Arg Glu Thr Asp
 35 40 45
 Glu Glu Pro Glu Glu Pro Gly Arg Arg Gly Ser Phe Val Glu Met Val
 50 55 60
 Asp Asn Leu Arg Gly Lys Ser Gly Gln Gly Tyr Tyr Val Glu Met Thr
 65 70 75 80
 Val Gly Ser Pro Pro Gln Thr Leu Asn Ile Leu Val Asp Thr Gly Ser
 85 90 95
 Ser Asn Phe Ala Val Gly Ala Ala Pro His Pro Phe Leu His Arg Tyr
 100 105 110
 Tyr Gln Arg Gln Leu Ser Ser Thr Tyr Arg Asp Leu Arg Lys Gly Val
 115 120 125
 Tyr Val Pro Tyr Thr Gln Gly Lys Trp Glu Gly Glu Leu Gly Thr Asp
 130 135 140
 Leu Val Ser Ile Pro His Gly Pro Asn Val Thr Val Arg Ala Asn Ile
 145 150 155 160
 Ala Ala Ile Thr Glu Ser Asp Lys Phe Phe Ile Asn Gly Ser Asn Trp
 165 170 175
 Glu Gly Ile Leu Gly Leu Ala Tyr Ala Glu Ile Ala Arg Pro Asp Asp
 180 185 190
 Ser Leu Glu Pro Phe Phe Asp Ser Leu Val Lys Gln Thr His Val Pro
 195 200 205
 Asn Leu Phe Ser Leu Gln Leu Cys Gly Ala Gly Phe Pro Leu Asn Gln
 210 215 220
 Ser Glu Val Leu Ala Ser Val Gly Gly Ser Met Ile Ile Gly Gly Ile
 225 230 235 240
 Asp His Ser Leu Tyr Thr Gly Ser Leu Trp Tyr Thr Pro Ile Arg Arg
 245 250 255
 Glu Trp Tyr Tyr Glu Val Ile Ile Val Arg Val Glu Ile Asn Gly Gln
 260 265 270
 Asp Leu Lys Met Asp Cys Lys Glu Tyr Asn Tyr Asp Lys Ser Ile Val
 275 280 285
 Asp Ser Gly Thr Thr Asn Leu Arg Leu Pro Lys Lys Val Phe Glu Ala
 290 295 300
 Ala Val Lys Ser Ile Lys Ala Ala Ser Ser Thr Glu Lys Phe Pro Asp
 305 310 315 320
 Gly Phe Trp Leu Gly Glu Gln Leu Val Cys Trp Gln Ala Gly Thr Thr
 325 330 335
 Pro Trp Asn Ile Phe Pro Val Ile Ser Leu Tyr Leu Met Gly Glu Val
 340 345 350
 Thr Asn Gln Ser Phe Arg Ile Thr Ile Leu Pro Gln Gln Tyr Leu Arg
 355 360 365
 Pro Val Glu Asp Val Ala Thr Ser Gln Asp Asp Cys Tyr Lys Phe Ala
 370 375 380
 Ile Ser Gln Ser Ser Thr Gly Thr Val Met Gly Ala Val Ile Met Glu
 385 390 395 400
 Gly Phe Tyr Val Val Phe Asp Arg Ala Arg Lys Arg Ile Gly Phe Ala
 405 410 415
 Val Ser Ala

<210> 58
 <211> 407
 <212> PRT
 <213> Homo sapiens

<400> 58
 Glu Thr Asp Glu Glu Pro Glu Glu Pro Gly Arg Arg Gly Ser Phe Val
 1 5 10 15
 Glu Met Val Asp Asn Leu Arg Gly Lys Ser Gly Gln Gly Tyr Tyr Val
 20 25 30

Glu Met Thr Val Gly Ser Pro Pro Gln Thr Leu Asn Ile Leu Val Asp
 35 40 45
 Thr Gly Ser Ser Asn Phe Ala Val Gly Ala Ala Pro His Pro Phe Leu
 50 55 60
 His Arg Tyr Tyr Gln Arg Gln Leu Ser Ser Thr Tyr Arg Asp Leu Arg
 65 70 75 80
 Lys Gly Val Tyr Val Pro Tyr Thr Gln Gly Lys Trp Glu Gly Glu Leu
 85 90 95
 Gly Thr Asp Leu Val Ser Ile Pro His Gly Pro Asn Val Thr Val Arg
 100 105 110
 Ala Asn Ile Ala Ala Ile Thr Glu Ser Asp Lys Phe Phe Ile Asn Gly
 115 120 125
 Ser Asn Trp Glu Gly Ile Leu Gly Leu Ala Tyr Ala Glu Ile Ala Arg
 130 135 140
 Pro Asp Asp Ser Leu Glu Pro Phe Phe Asp Ser Leu Val Lys Gln Thr
 145 150 155 160
 His Val Pro Asn Leu Phe Ser Leu Gln Leu Cys Gly Ala Gly Phe Pro
 165 170 175
 Leu Asn Gln Ser Glu Val Leu Ala Ser Val Gly Gly Ser Met Ile Ile
 180 185 190
 Gly Gly Ile Asp His Ser Leu Tyr Thr Gly Ser Leu Trp Tyr Thr Pro
 195 200 205
 Ile Arg Arg Glu Trp Tyr Tyr Glu Val Ile Ile Val Arg Val Glu Ile
 210 215 220
 Asn Gly Gln Asp Leu Lys Met Asp Cys Lys Glu Tyr Asn Tyr Asp Lys
 225 230 235 240
 Ser Ile Val Asp Ser Gly Thr Thr Asn Leu Arg Leu Pro Lys Lys Val
 245 250 255
 Phe Glu Ala Ala Val Lys Ser Ile Lys Ala Ala Ser Ser Thr Glu Lys
 260 265 270
 Phe Pro Asp Gly Phe Trp Leu Gly Gln Gln Leu Val Cys Trp Gln Ala
 275 280 285
 Gly Thr Thr Pro Trp Asn Ile Phe Pro Val Ile Ser Leu Tyr Leu Met
 290 295 300
 Gly Glu Val Thr Asn Gln Ser Phe Arg Ile Thr Ile Leu Pro Gln Gln
 305 310 315 320
 Tyr Leu Arg Pro Val Glu Asp Val Ala Thr Ser Gln Asp Asp Cys Tyr
 325 330 335
 Lys Phe Ala Ile Ser Gln Ser Ser Thr Gly Thr Val Met Gly Ala Val
 340 345 350
 Ile Met Glu Gly Phe Tyr Val Val Phe Asp Arg Ala Arg Lys Arg Ile
 355 360 365
 Gly Phe Ala Val Ser Ala Cys His Val His Asp Glu Phe Arg Thr Ala
 370 375 380
 Ala Val Glu Gly Pro Phe Val Thr Leu Asp Met Glu Asp Cys Gly Tyr
 385 390 395 400
 Asn Ile Pro Gln Thr Asp Glu
 405

<210> 59
 <211> 452
 <212> PRT
 <213> Homo sapiens

<400> 59
 Met Ala Gln Ala Leu Pro Trp Leu Leu Leu Trp Met Gly Ala Gly Val
 1 5 10 15
 Leu Pro Ala His Gly Thr Gln His Gly Ile Arg Leu Pro Leu Arg Ser
 20 25 30

Gly Leu Gly Gly Ala Pro Leu Gly Leu Arg Leu Pro Arg Glu Thr Asp
 35 40 45
 Glu Glu Pro Glu Glu Pro Gly Arg Arg Gly Ser Phe Val Glu Met Val
 50 55 60
 Asp Asn Leu Arg Gly Lys Ser Gly Gln Gly Tyr Tyr Val Glu Met Thr
 65 70 75 80
 Val Gly Ser Pro Pro Gln Thr Leu Asn Ile Leu Val Asp Thr Gly Ser
 85 90 95
 Ser Asn Phe Ala Val Gly Ala Ala Pro His Pro Phe Leu His Arg Tyr
 100 105 110
 Tyr Gln Arg Gln Leu Ser Ser Thr Tyr Arg Asp Leu Arg Lys Gly Val
 115 120 125
 Tyr Val Pro Tyr Thr Gln Gly Lys Trp Glu Gly Glu Leu Gly Thr Asp
 130 135 140
 Leu Val Ser Ile Pro His Gly Pro Asn Val Thr Val Arg Ala Asn Ile
 145 150 155 160
 Ala Ala Ile Thr Glu Ser Asp Lys Phe Phe Ile Asn Gly Ser Asn Trp
 165 170 175
 Glu Gly Ile Leu Gly Leu Ala Tyr Ala Gln Ile Ala Arg Pro Asp Asp
 180 185 190
 Ser Leu Glu Pro Phe Phe Asp Ser Leu Val Lys Gln Thr His Val Pro
 195 200 205
 Asn Leu Phe Ser Leu Gln Leu Cys Gly Ala Gly Phe Pro Leu Asn Gln
 210 215 220
 Ser Glu Val Leu Ala Ser Val Gly Gly Ser Met Ile Ile Gly Gly Ile
 225 230 235 240
 Asp His Ser Leu Tyr Thr Gly Ser Leu Trp Tyr Thr Pro Ile Arg Arg
 245 250 255
 Glu Trp Tyr Tyr Glu Val Ile Ile Val Arg Val Glu Ile Asn Gly Gln
 260 265 270
 Asp Leu Lys Met Asp Cys Lys Glu Tyr Asn Tyr Asp Lys Ser Ile Val
 275 280 285
 Asp Ser Gly Thr Thr Asn Leu Arg Leu Pro Lys Lys Val Phe Glu Ala
 290 295 300
 Ala Val Lys Ser Ile Lys Ala Ala Ser Ser Thr Glu Lys Phe Pro Asp
 305 310 315 320
 Gly Phe Trp Leu Gly Gln Gln Leu Val Cys Trp Gln Ala Gly Thr Thr
 325 330 335
 Pro Trp Asn Ile Phe Pro Val Ile Ser Leu Tyr Leu Met Gly Glu Val
 340 345 350
 Thr Asn Gln Ser Phe Arg Ile Thr Ile Leu Pro Gln Gln Tyr Leu Arg
 355 360 365
 Pro Val Glu Asp Val Ala Thr Ser Gln Asp Asp Cys Tyr Lys Phe Ala
 370 375 380
 Ile Ser Gln Ser Ser Thr Gly Thr Val Met Gly Ala Val Ile Met Glu
 385 390 395 400
 Gly Phe Tyr Val Val Phe Asp Arg Ala Arg Lys Arg Ile Gly Phe Ala
 405 410 415
 Val Ser Ala Cys His Val His Asp Glu Phe Arg Thr Ala Ala Val Glu
 420 425 430
 Gly Pro Phe Val Thr Leu Asp Met Glu Asp Cys Gly Tyr Asn Ile Pro
 435 440 445
 Gln Thr Asp Glu
 450

<210> 60
 <211> 420
 <212> PRT
 <213> Homo sapiens

<400> 60

Met Ala Gln Ala Leu Pro Trp Leu Leu Leu Trp Met Gly Ala Gly Val
 1 5 10 15
 Leu Pro Ala His Gly Thr Gln His Gly Ile Arg Leu Pro Leu Arg Ser
 20 25 30
 Gly Leu Gly Gly Ala Pro Leu Gly Leu Arg Leu Pro Arg Glu Thr Asp
 35 40 45
 Glu Glu Pro Glu Glu Pro Gly Arg Arg Gly Ser Phe Val Glu Met Val
 50 55 60
 Asp Asn Leu Arg Gly Lys Ser Gly Gln Gly Tyr Tyr Val Glu Met Thr
 65 70 75 80
 Val Gly Ser Pro Pro Gln Thr Leu Asn Ile Leu Val Asp Thr Gly Ser
 85 90 95
 Ser Asn Phe Ala Val Gly Ala Ala Pro His Pro Phe Leu His Arg Tyr
 100 105 110
 Tyr Gln Arg Gln Leu Ser Ser Thr Tyr Arg Asp Leu Arg Lys Gly Val
 115 120 125
 Tyr Val Pro Tyr Thr Gln Gly Lys Trp Glu Gly Glu Leu Gly Thr Asp
 130 135 140
 Leu Val Ser Ile Pro His Gly Pro Asn Val Thr Val Arg Ala Asn Ile
 145 150 155 160
 Ala Ala Ile Thr Glu Ser Asp Lys Phe Phe Ile Asn Gly Ser Asn Trp
 165 170 175
 Glu Gly Ile Leu Gly Leu Ala Tyr Ala Glu Ile Ala Arg Pro Asp Asp
 180 185 190
 Ser Leu Glu Pro Phe Phe Asp Ser Leu Val Lys Gln Thr His Val Pro
 195 200 205
 Asn Leu Phe Ser Leu Gln Leu Cys Gly Ala Gly Phe Pro Leu Asn Gln
 210 215 220
 Ser Glu Val Leu Ala Ser Val Gly Gly Ser Met Ile Ile Gly Gly Ile
 225 230 235 240
 Asp His Ser Leu Tyr Thr Gly Ser Leu Trp Tyr Thr Pro Ile Arg Arg
 245 250 255
 Glu Trp Tyr Tyr Glu Val Ile Ile Val Arg Val Glu Ile Asn Gly Gln
 260 265 270
 Asp Leu Lys Met Asp Cys Lys Glu Tyr Asn Tyr Asp Lys Ser Ile Val
 275 280 285
 Asp Ser Gly Thr Thr Asn Leu Arg Leu Pro Lys Lys Val Phe Glu Ala
 290 295 300
 Ala Val Lys Ser Ile Lys Ala Ala Ser Ser Thr Glu Lys Phe Pro Asp
 305 310 315 320
 Gly Phe Trp Leu Gly Glu Gln Leu Val Cys Trp Gln Ala Gly Thr Thr
 325 330 335
 Pro Trp Asn Ile Phe Pro Val Ile Ser Leu Tyr Leu Met Gly Glu Val
 340 345 350
 Thr Asn Gln Ser Phe Arg Ile Thr Ile Leu Pro Gln Gln Tyr Leu Arg
 355 360 365
 Pro Val Glu Asp Val Ala Thr Ser Gln Asp Asp Cys Tyr Lys Phe Ala
 370 375 380
 Ile Ser Gln Ser Ser Thr Gly Thr Val Met Gly Ala Val Ile Met Glu
 385 390 395 400
 Gly Phe Tyr Val Val Phe Asp Arg Ala Arg Lys Arg Ile Gly Phe Ala
 405 410 415
 Val Ser Ala Cys
 420

<210> 61

<211> 7

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic peptide inhibitor

<220>

<221> MOD_RES

<222> 4

<223> Xaa = hydroxyethylene

<400> 61

Glu Val Met Xaa Ala Glu Phe
1 5

<210> 62

<211> 26

<212> PRT

<213> Homo sapiens

<400> 62

Leu Met Thr Ile Ala Tyr Val Met Ala Ala Ile Cys Ala Leu Phe Met
1 5 10 15
Leu Pro Leu Cys Leu Met Val Cys Gln Trp
20 25

<210> 63

<211> 33

<212> PRT

<213> Homo sapiens

<220>

<223> P26-P4'sw peptide substrate

<400> 63

Cys Gly Gly Ala Asp Arg Gly Leu Thr Thr Arg Pro Gly Ser Gly Leu
1 5 10 15
Thr Asn Ile Lys Thr Glu Glu Ile Ser Glu Val Asn Leu Asp Ala Glu
20 25 30
Phe

<210> 64

<211> 29

<212> PRT

<213> Homo sapiens

<220>

<223> P26-P1' peptide substrate with CGG linker

<400> 64

Cys Gly Gly Ala Asp Arg Gly Leu Thr Thr Arg Pro Gly Ser Gly Leu
1 5 10 15
Thr Asn Ile Lys Thr Glu Glu Ile Ser Glu Val Asn Leu
20 25

<210> 65

<211> 501

<212> PRT

<213> Mus musculus

<400> 65

Met Ala Pro Ala Leu His Trp Leu Leu Leu Trp Val Gly Ser Gly Met
1 5 10 15

Leu Pro Ala Gln Gly Thr His Leu Gly Ile Arg Leu Pro Leu Arg Ser
 20 25 30
 Gly Leu Ala Gly Pro Pro Leu Gly Leu Arg Leu Pro Arg Glu Thr Asp
 35 40 45
 Glu Glu Ser Glu Glu Pro Gly Arg Arg Gly Ser Phe Val Glu Met Val
 50 55 60
 Asp Asn Leu Arg Gly Lys Ser Gly Gln Gly Tyr Tyr Val Glu Met Thr
 65 70 75 80
 Val Gly Ser Pro Pro Gln Thr Leu Asn Ile Leu Val Asp Thr Gly Ser
 85 90 95
 Ser Asn Phe Ala Val Gly Ala Ala Pro His Pro Phe Leu His Arg Tyr
 100 105 110
 Tyr Gln Arg Gln Leu Ser Ser Thr Tyr Arg Asp Leu Arg Lys Gly Val
 115 120 125
 Tyr Val Pro Tyr Thr Gln Gly Lys Trp Glu Gly Glu Leu Gly Thr Asp
 130 135 140
 Leu Val Ser Ile Pro His Gly Pro Asn Val Thr Val Arg Ala Asn Ile
 145 150 155 160
 Ala Ala Ile Thr Glu Ser Asp Lys Phe Phe Ile Asn Gly Ser Asn Trp
 165 170 175
 Glu Gly Ile Leu Gly Leu Ala Tyr Ala Glu Ile Ala Arg Pro Asp Asp
 180 185 190
 Ser Leu Glu Pro Phe Phe Asp Ser Leu Val Lys Gln Thr His Ile Pro
 195 200 205
 Asn Ile Phe Ser Leu Gln Leu Cys Gly Ala Gly Phe Pro Leu Asn Gln
 210 215 220
 Thr Glu Ala Leu Ala Ser Val Gly Gly Ser Met Ile Ile Gly Gly Ile
 225 230 235 240
 Asp His Ser Leu Tyr Thr Gly Ser Leu Trp Tyr Thr Pro Ile Arg Arg
 245 250 255
 Glu Trp Tyr Tyr Glu Val Ile Ile Val Arg Val Glu Ile Asn Gly Gln
 260 265 270
 Asp Leu Lys Met Asp Cys Lys Glu Tyr Asn Tyr Asp Lys Ser Ile Val
 275 280 285
 Asp Ser Gly Thr Thr Asn Leu Arg Leu Pro Lys Lys Val Phe Glu Ala
 290 295 300
 Ala Val Lys Ser Ile Lys Ala Ala Ser Ser Thr Glu Lys Phe Pro Asp
 305 310 315 320
 Gly Phe Trp Leu Gly Glu Gln Leu Val Cys Trp Gln Ala Gly Thr Thr
 325 330 335
 Pro Trp Asn Ile Phe Pro Val Ile Ser Leu Tyr Leu Met Gly Glu Val
 340 345 350
 Thr Asn Gln Ser Phe Arg Ile Thr Ile Leu Pro Gln Gln Tyr Leu Arg
 355 360 365
 Pro Val Glu Asp Val Ala Thr Ser Gln Asp Asp Cys Tyr Lys Phe Ala
 370 375 380
 Val Ser Gln Ser Ser Thr Gly Thr Val Met Gly Ala Val Ile Met Glu
 385 390 395 400
 Gly Phe Tyr Val Val Phe Asp Arg Ala Arg Lys Arg Ile Gly Phe Ala
 405 410 415
 Val Ser Ala Cys His Val His Asp Glu Phe Arg Thr Ala Ala Val Glu
 420 425 430
 Gly Pro Phe Val Thr Ala Asp Met Glu Asp Cys Gly Tyr Asn Ile Pro
 435 440 445
 Gln Thr Asp Glu Ser Thr Leu Met Thr Ile Ala Tyr Val Met Ala Ala
 450 455 460
 Ile Cys Ala Leu Phe Met Leu Pro Leu Cys Leu Met Val Cys Gln Trp
 465 470 475 480
 Arg Cys Leu Arg Cys Leu Arg His Gln His Asp Asp Phe Gly Asp Asp
 485 490 495

Ile Ser Leu Leu Lys
500

<210> 66
<211> 480
<212> PRT
<213> Homo sapiens

<400> 66
Thr Gln His Gly Ile Arg Leu Pro Leu Arg Ser Gly Leu Gly Gly Ala
1 5 10 15
Pro Leu Gly Leu Arg Leu Pro Arg Glu Thr Asp Glu Glu Pro Glu Glu
20 25 30
Pro Gly Arg Arg Gly Ser Phe Val Glu Met Val Asp Asn Leu Arg Gly
35 40 45
Lys Ser Gly Gln Gly Tyr Tyr Val Glu Met Thr Val Gly Ser Pro Pro
50 55 60
Gln Thr Leu Asn Ile Leu Val Asp Thr Gly Ser Ser Asn Phe Ala Val
65 70 75 80
Gly Ala Ala Pro His Pro Phe Leu His Arg Tyr Tyr Gln Arg Gln Leu
85 90 95
Ser Ser Thr Tyr Arg Asp Leu Arg Lys Gly Val Tyr Val Pro Tyr Thr
100 105 110
Gln Gly Lys Trp Glu Gly Glu Leu Gly Thr Asp Leu Val Ser Ile Pro
115 120 125
His Gly Pro Asn Val Thr Val Arg Ala Asn Ile Ala Ala Ile Thr Glu
130 135 140
Ser Asp Lys Phe Phe Ile Asn Gly Ser Asn Trp Glu Gly Ile Leu Gly
145 150 155 160
Leu Ala Tyr Ala Glu Ile Ala Arg Pro Asp Asp Ser Leu Glu Pro Phe
165 170 175
Phe Asp Ser Leu Val Lys Gln Thr His Val Pro Asn Leu Phe Ser Leu
180 185 190
Gln Leu Cys Gly Ala Gly Phe Pro Leu Asn Gln Ser Glu Val Leu Ala
195 200 205
Ser Val Gly Gly Ser Met Ile Ile Gly Gly Ile Asp His Ser Leu Tyr
210 215 220
Thr Gly Ser Leu Trp Tyr Thr Pro Ile Arg Arg Glu Trp Tyr Tyr Glu
225 230 235 240
Val Ile Ile Val Arg Val Glu Ile Asn Gly Gln Asp Leu Lys Met Asp
245 250 255
Cys Lys Glu Tyr Asn Tyr Asp Lys Ser Ile Val Asp Ser Gly Thr Thr
260 265 270
Asn Leu Arg Leu Pro Lys Lys Val Phe Glu Ala Ala Val Lys Ser Ile
275 280 285
Lys Ala Ala Ser Ser Thr Glu Lys Phe Pro Asp Gly Phe Trp Leu Gly
290 295 300
Glu Gln Leu Val Cys Trp Gln Ala Gly Thr Thr Pro Trp Asn Ile Phe
305 310 315 320
Pro Val Ile Ser Leu Tyr Leu Met Gly Glu Val Thr Asn Gln Ser Phe
325 330 335
Arg Ile Thr Ile Leu Pro Gln Gln Tyr Leu Arg Pro Val Glu Asp Val
340 345 350
Ala Thr Ser Gln Asp Asp Cys Tyr Lys Phe Ala Ile Ser Gln Ser Ser
355 360 365
Thr Gly Thr Val Met Gly Ala Val Ile Met Glu Gly Phe Tyr Val Val
370 375 380
Phe Asp Arg Ala Arg Lys Arg Ile Gly Phe Ala Val Ser Ala Cys His
385 390 395 400
Val His Asp Glu Phe Arg Thr Ala Ala Val Glu Gly Pro Phe Val Thr
405 410 415

Leu Asp Met Glu Asp Cys Gly Tyr Asn Ile Pro Gln Thr Asp Glu Ser
 420 425 430
 Thr Leu Met Thr Ile Ala Tyr Val Met Ala Ala Ile Cys Ala Leu Phe
 435 440 445
 Met Leu Pro Leu Cys Leu Met Val Cys Gln Trp Arg Cys Leu Arg Cys
 450 455 460
 Leu Arg Gln Gln His Asp Asp Phe Ala Asp Asp Ile Ser Leu Leu Lys
 465 470 475 480

<210> 67

<211> 444

<212> PRT

<213> Homo sapiens

<400> 67

Gly Ser Phe Val Glu Met Val Asp Asn Leu Arg Gly Lys Ser Gly Gln
 1 5 10 15
 Gly Tyr Tyr Val Glu Met Thr Val Gly Ser Pro Pro Gln Thr Leu Asn
 20 25 30
 Ile Leu Val Asp Thr Gly Ser Ser Asn Phe Ala Val Gly Ala Ala Pro
 35 40 45
 His Pro Phe Leu His Arg Tyr Tyr Gln Arg Gln Leu Ser Ser Thr Tyr
 50 55 60
 Arg Asp Leu Arg Lys Gly Val Tyr Val Pro Tyr Thr Gln Gly Lys Trp
 65 70 75 80
 Glu Gly Glu Leu Gly Thr Asp Leu Val Ser Ile Pro His Gly Pro Asn
 85 90 95
 Val Thr Val Arg Ala Asn Ile Ala Ala Ile Thr Glu Ser Asp Lys Phe
 100 105 110
 Phe Ile Asn Gly Ser Asn Trp Glu Gly Ile Leu Gly Leu Ala Tyr Ala
 115 120 125
 Glu Ile Ala Arg Pro Asp Asp Ser Leu Glu Pro Phe Phe Asp Ser Leu
 130 135 140
 Val Lys Gln Thr His Val Pro Asn Leu Phe Ser Leu Gln Leu Cys Gly
 145 150 155 160
 Ala Gly Phe Pro Leu Asn Gln Ser Glu Val Leu Ala Ser Val Gly Gly
 165 170 175
 Ser Met Ile Ile Gly Gly Ile Asp His Ser Leu Tyr Thr Gly Ser Leu
 180 185 190
 Trp Tyr Thr Pro Ile Arg Arg Glu Trp Tyr Tyr Glu Val Ile Ile Val
 195 200 205
 Arg Val Glu Ile Asn Gly Gln Asp Leu Lys Met Asp Cys Lys Glu Tyr
 210 215 220
 Asn Tyr Asp Lys Ser Ile Val Asp Ser Gly Thr Thr Asn Leu Arg Leu
 225 230 235 240
 Pro Lys Lys Val Phe Glu Ala Ala Val Lys Ser Ile Lys Ala Ala Ser
 245 250 255
 Ser Thr Glu Lys Phe Pro Asp Gly Phe Trp Leu Gly Glu Gln Leu Val
 260 265 270
 Cys Trp Gln Ala Gly Thr Thr Pro Trp Asn Ile Phe Pro Val Ile Ser
 275 280 285
 Leu Tyr Leu Met Gly Glu Val Thr Asn Gln Ser Phe Arg Ile Thr Ile
 290 295 300
 Leu Pro Gln Gln Tyr Leu Arg Pro Val Glu Asp Val Ala Thr Ser Gln
 305 310 315 320
 Asp Asp Cys Tyr Lys Phe Ala Ile Ser Gln Ser Ser Thr Gly Thr Val
 325 330 335
 Met Gly Ala Val Ile Met Glu Gly Phe Tyr Val Val Phe Asp Arg Ala
 340 345 350
 Arg Lys Arg Ile Gly Phe Ala Val Ser Ala Cys His Val His Asp Glu

Met Gly Ala Val Ile Met Glu Gly Phe Tyr Val Val Phe Asp Arg Ala
 340 345 350
 Arg Lys Arg Ile Gly Phe Ala Val Ser Ala Cys His Val His Asp Glu
 355 360 365
 Phe Arg Thr Ala Ala Val Glu Gly Pro Phe Val Thr Leu Asp Met Glu
 370 375 380
 Asp Cys Gly Tyr Asn Ile Pro Gln Thr Asp Glu
 385 390 395

<210> 69
 <211> 439
 <212> PRT
 <213> Homo sapiens

<400> 69
 Met Val Asp Asn Leu Arg Gly Lys Ser Gly Gln Gly Tyr Tyr Val Glu
 1 5 10 15
 Met Thr Val Gly Ser Pro Pro Gln Thr Leu Asn Ile Leu Val Asp Thr
 20 25 30
 Gly Ser Ser Asn Phe Ala Val Gly Ala Ala Pro His Pro Phe Leu His
 35 40 45
 Arg Tyr Tyr Gln Arg Gln Leu Ser Ser Thr Tyr Arg Asp Leu Arg Lys
 50 55 60
 Gly Val Tyr Val Pro Tyr Thr Gln Gly Lys Trp Glu Gly Glu Leu Gly
 65 70 75 80
 Thr Asp Leu Val Ser Ile Pro His Gly Pro Asn Val Thr Val Arg Ala
 85 90 95
 Asn Ile Ala Ala Ile Thr Glu Ser Asp Lys Phe Phe Ile Asn Gly Ser
 100 105 110
 Asn Trp Glu Gly Ile Leu Gly Leu Ala Tyr Ala Glu Ile Ala Arg Pro
 115 120 125
 Asp Asp Ser Leu Glu Pro Phe Phe Asp Ser Leu Val Lys Gln Thr His
 130 135 140
 Val Pro Asn Leu Phe Ser Leu Gln Leu Cys Gly Ala Gly Phe Pro Leu
 145 150 155 160
 Asn Gln Ser Glu Val Leu Ala Ser Val Gly Gly Ser Met Ile Ile Gly
 165 170 175
 Gly Ile Asp His Ser Leu Tyr Thr Gly Ser Leu Trp Tyr Thr Pro Ile
 180 185 190
 Arg Arg Glu Trp Tyr Tyr Glu Val Ile Ile Val Arg Val Glu Ile Asn
 195 200 205
 Gly Gln Asp Leu Lys Met Asp Cys Lys Glu Tyr Asn Tyr Asp Lys Ser
 210 215 220
 Ile Val Asp Ser Gly Thr Thr Asn Leu Arg Leu Pro Lys Lys Val Phe
 225 230 235 240
 Glu Ala Ala Val Lys Ser Ile Lys Ala Ala Ser Ser Thr Glu Lys Phe
 245 250 255
 Pro Asp Gly Phe Trp Leu Gly Glu Gln Leu Val Cys Trp Gln Ala Gly
 260 265 270
 Thr Thr Pro Trp Asn Ile Phe Pro Val Ile Ser Leu Tyr Leu Met Gly
 275 280 285
 Glu Val Thr Asn Gln Ser Phe Arg Ile Thr Ile Leu Pro Gln Gln Tyr
 290 295 300
 Leu Arg Pro Val Glu Asp Val Ala Thr Ser Gln Asp Asp Cys Tyr Lys
 305 310 315 320
 Phe Ala Ile Ser Gln Ser Ser Thr Gly Thr Val Met Gly Ala Val Ile
 325 330 335
 Met Glu Gly Phe Tyr Val Val Phe Asp Arg Ala Arg Lys Arg Ile Gly
 340 345 350
 Phe Ala Val Ser Ala Cys His Val His Asp Glu Phe Arg Thr Ala Ala
 355 360 365

Val Glu Gly Pro Phe Val Thr Leu Asp Met Glu Asp Cys Gly Tyr Asn
 370 375 380
 Ile Pro Gln Thr Asp Glu Ser Thr Leu Met Thr Ile Ala Tyr Val Met
 385 390 395 400
 Ala Ala Ile Cys Ala Leu Phe Met Leu Pro Leu Cys Leu Met Val Cys
 405 410 415
 Gln Trp Arg Cys Leu Arg Cys Leu Arg Gln Gln His Asp Asp Phe Ala
 420 425 430
 Asp Asp Ile Ser Leu Leu Lys
 435

<210> 70
 <211> 390
 <212> PRT
 <213> Homo sapiens

<400> 70
 Met Val Asp Asn Leu Arg Gly Lys Ser Gly Gln Gly Tyr Tyr Val Glu
 1 5 10 15
 Met Thr Val Gly Ser Pro Pro Gln Thr Leu Asn Ile Leu Val Asp Thr
 20 25 30
 Gly Ser Ser Asn Phe Ala Val Gly Ala Ala Pro His Pro Phe Leu His
 35 40 45
 Arg Tyr Tyr Gln Arg Gln Leu Ser Ser Thr Tyr Arg Asp Leu Arg Lys
 50 55 60
 Gly Val Tyr Val Pro Tyr Thr Gln Gly Lys Trp Glu Gly Glu Leu Gly
 65 70 75 80
 Thr Asp Leu Val Ser Ile Pro His Gly Pro Asn Val Thr Val Arg Ala
 85 90 95
 Asn Ile Ala Ala Ile Thr Glu Ser Asp Lys Phe Phe Ile Asn Gly Ser
 100 105 110
 Asn Trp Glu Gly Ile Leu Gly Leu Ala Tyr Ala Glu Ile Ala Arg Pro
 115 120 125
 Asp Asp Ser Leu Glu Pro Phe Phe Asp Ser Leu Val Lys Gln Thr His
 130 135 140
 Val Pro Asn Leu Phe Ser Leu Gln Leu Cys Gly Ala Gly Phe Pro Leu
 145 150 155 160
 Asn Gln Ser Glu Val Leu Ala Ser Val Gly Gly Ser Met Ile Ile Gly
 165 170 175
 Gly Ile Asp His Ser Leu Tyr Thr Gly Ser Leu Trp Tyr Thr Pro Ile
 180 185 190
 Arg Arg Glu Trp Tyr Tyr Glu Val Ile Ile Val Arg Val Glu Ile Asn
 195 200 205
 Gly Gln Asp Leu Lys Met Asp Cys Lys Glu Tyr Asn Tyr Asp Lys Ser
 210 215 220
 Ile Val Asp Ser Gly Thr Thr Asn Leu Arg Leu Pro Lys Lys Val Phe
 225 230 235 240
 Glu Ala Ala Val Lys Ser Ile Lys Ala Ala Ser Ser Thr Glu Lys Phe
 245 250 255
 Pro Asp Gly Phe Trp Leu Gly Glu Gln Leu Val Cys Trp Gln Ala Gly
 260 265 270
 Thr Thr Pro Trp Asn Ile Phe Pro Val Ile Ser Leu Tyr Leu Met Gly
 275 280 285
 Glu Val Thr Asn Gln Ser Phe Arg Ile Thr Ile Leu Pro Gln Gln Tyr
 290 295 300
 Leu Arg Pro Val Glu Asp Val Ala Thr Ser Gln Asp Asp Cys Tyr Lys
 305 310 315 320
 Phe Ala Ile Ser Gln Ser Ser Thr Gly Thr Val Met Gly Ala Val Ile
 325 330 335
 Met Glu Gly Phe Tyr Val Val Phe Asp Arg Ala Arg Lys Arg Ile Gly
 340 345 350

Phe Ala Val Ser Ala Cys His Val His Asp Glu Phe Arg Thr Ala Ala
 355 360 365
 Val Glu Gly Pro Phe Val Thr Leu Asp Met Glu Asp Cys Gly Tyr Asn
 370 375 380
 Ile Pro Gln Thr Asp Glu
 385 390

<210> 71
 <211> 374
 <212> PRT
 <213> Homo sapiens

<400> 71
 Glu Thr Asp Glu Glu Pro Glu Glu Pro Gly Arg Arg Gly Ser Phe Val
 1 5 10 15
 Glu Met Val Asp Asn Leu Arg Gly Lys Ser Gly Gln Gly Tyr Tyr Val
 20 25 30
 Glu Met Thr Val Gly Ser Pro Pro Gln Thr Leu Asn Ile Leu Val Asp
 35 40 45
 Thr Gly Ser Ser Asn Phe Ala Val Gly Ala Ala Pro His Pro Phe Leu
 50 55 60
 His Arg Tyr Tyr Gln Arg Gln Leu Ser Ser Thr Tyr Arg Asp Leu Arg
 65 70 75 80
 Lys Gly Val Tyr Val Pro Tyr Thr Gln Gly Lys Trp Glu Gly Glu Leu
 85 90 95
 Gly Thr Asp Leu Val Ser Ile Pro His Gly Pro Asn Val Thr Val Arg
 100 105 110
 Ala Asn Ile Ala Ala Ile Thr Glu Ser Asp Lys Phe Phe Ile Asn Gly
 115 120 125
 Ser Asn Trp Glu Gly Ile Leu Gly Leu Ala Tyr Ala Glu Ile Ala Arg
 130 135 140
 Pro Asp Asp Ser Leu Glu Pro Phe Phe Asp Ser Leu Val Lys Gln Thr
 145 150 155 160
 His Val Pro Asn Leu Phe Ser Leu Gln Leu Cys Gly Ala Gly Phe Pro
 165 170 175
 Leu Asn Gln Ser Glu Val Leu Ala Ser Val Gly Gly Ser Met Ile Ile
 180 185 190
 Gly Gly Ile Asp His Ser Leu Tyr Thr Gly Ser Leu Trp Tyr Thr Pro
 195 200 205
 Ile Arg Arg Glu Trp Tyr Tyr Glu Val Ile Ile Val Arg Val Glu Ile
 210 215 220
 Asn Gly Gln Asp Leu Lys Met Asp Cys Lys Glu Tyr Asn Tyr Asp Lys
 225 230 235 240
 Ser Ile Val Asp Ser Gly Thr Thr Asn Leu Arg Leu Pro Lys Lys Val
 245 250 255
 Phe Glu Ala Ala Val Lys Ser Ile Lys Ala Ala Ser Ser Thr Glu Lys
 260 265 270
 Phe Pro Asp Gly Phe Trp Leu Gly Glu Gln Leu Val Cys Trp Gln Ala
 275 280 285
 Gly Thr Thr Pro Trp Asn Ile Phe Pro Val Ile Ser Leu Tyr Leu Met
 290 295 300
 Gly Glu Val Thr Asn Gln Ser Phe Arg Ile Thr Ile Leu Pro Gln Gln
 305 310 315 320
 Tyr Leu Arg Pro Val Glu Asp Val Ala Thr Ser Gln Asp Asp Cys Tyr
 325 330 335
 Lys Phe Ala Ile Ser Gln Ser Ser Thr Gly Thr Val Met Gly Ala Val
 340 345 350
 Ile Met Glu Gly Phe Tyr Val Val Phe Asp Arg Ala Arg Lys Arg Ile
 355 360 365
 Gly Phe Ala Val Ser Ala
 370

<210> 72
<211> 14
<212> PRT
<213> Artificial Sequence

<220>
<223> P10-P4'staD-V peptide inhibitor

<220>
<221> MOD_RES
<222> 10
<223> Xaa is statine moiety

<400> 72
Lys Thr Glu Glu Ile Ser Glu Val Asn Xaa Val Ala Glu Phe
1 5 10

<210> 73
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> P4-P4'staD-V peptide inhibitor

<220>
<221> MOD_RES
<222> 5
<223> Xaa is statine moiety

<400> 73
Ser Glu Val Asn Xaa Val Ala Glu Phe
1 5

<210> 74
<211> 431
<212> PRT
<213> Homo sapiens

<400> 74
Thr Gln His Gly Ile Arg Leu Pro Leu Arg Ser Gly Leu Gly Gly Ala
1 5 10 15
Pro Leu Gly Leu Arg Leu Pro Arg Glu Thr Asp Glu Glu Pro Glu Glu
20 25 30
Pro Gly Arg Arg Gly Ser Phe Val Glu Met Val Asp Asn Leu Arg Gly
35 40 45
Lys Ser Gly Gln Gly Tyr Tyr Val Glu Met Thr Val Gly Ser Pro Pro
50 55 60
Gln Thr Leu Asn Ile Leu Val Asp Thr Gly Ser Ser Asn Phe Ala Val
65 70 75 80
Gly Ala Ala Pro His Pro Phe Leu His Arg Tyr Tyr Gln Arg Gln Leu
85 90 95
Ser Ser Thr Tyr Arg Asp Leu Arg Lys Gly Val Tyr Val Pro Tyr Thr
100 105 110
Gln Gly Lys Trp Glu Gly Glu Leu Gly Thr Asp Leu Val Ser Ile Pro
115 120 125
His Gly Pro Asn Val Thr Val Arg Ala Asn Ile Ala Ala Ile Thr Glu
130 135 140
Ser Asp Lys Phe Phe Ile Asn Gly Ser Asn Trp Glu Gly Ile Leu Gly
145 150 155 160

Leu Ala Tyr Ala Glu Ile Ala Arg Pro Asp Asp Ser Leu Glu Pro Phe
 165 170 175
 Phe Asp Ser Leu Val Lys Gln Thr His Val Pro Asn Leu Phe Ser Leu
 180 185 190
 Gln Leu Cys Gly Ala Gly Phe Pro Leu Asn Gln Ser Glu Val Leu Ala
 195 200 205
 Ser Val Gly Gly Ser Met Ile Ile Gly Gly Ile Asp His Ser Leu Tyr
 210 215 220
 Thr Gly Ser Leu Trp Tyr Thr Pro Ile Arg Arg Glu Trp Tyr Tyr Glu
 225 230 235 240
 Val Ile Ile Val Arg Val Glu Ile Asn Gly Gln Asp Leu Lys Met Asp
 245 250 255
 Cys Lys Glu Tyr Asn Tyr Asp Lys Ser Ile Val Asp Ser Gly Thr Thr
 260 265 270
 Asn Leu Arg Leu Pro Lys Lys Val Phe Glu Ala Ala Val Lys Ser Ile
 275 280 285
 Lys Ala Ala Ser Ser Thr Glu Lys Phe Pro Asp Gly Phe Trp Leu Gly
 290 295 300
 Glu Gln Leu Val Cys Trp Gln Ala Gly Thr Thr Pro Trp Asn Ile Phe
 305 310 315 320
 Pro Val Ile Ser Leu Tyr Leu Met Gly Glu Val Thr Asn Gln Ser Phe
 325 330 335
 Arg Ile Thr Ile Leu Pro Gln Gln Tyr Leu Arg Pro Val Glu Asp Val
 340 345 350
 Ala Thr Ser Gln Asp Asp Cys Tyr Lys Phe Ala Ile Ser Gln Ser Ser
 355 360 365
 Thr Gly Thr Val Met Gly Ala Val Ile Met Glu Gly Phe Tyr Val Val
 370 375 380
 Phe Asp Arg Ala Arg Lys Arg Ile Gly Phe Ala Val Ser Ala Cys His
 385 390 395 400
 Val His Asp Glu Phe Arg Thr Ala Ala Val Glu Gly Pro Phe Val Thr
 405 410 415
 Leu Asp Met Glu Asp Cys Gly Tyr Asn Ile Pro Gln Thr Asp Glu
 420 425 430

<210> 75
 <211> 361
 <212> PRT
 <213> Homo sapiens

<400> 75
 Met Val Asp Asn Leu Arg Gly Lys Ser Gly Gln Gly Tyr Tyr Val Glu
 1 5 10 15
 Met Thr Val Gly Ser Pro Pro Gln Thr Leu Asn Ile Leu Val Asp Thr
 20 25 30
 Gly Ser Ser Asn Phe Ala Val Gly Ala Ala Pro His Pro Phe Leu His
 35 40 45
 Arg Tyr Tyr Gln Arg Gln Leu Ser Ser Thr Tyr Arg Asp Leu Arg Lys
 50 55 60
 Gly Val Tyr Val Pro Tyr Thr Gln Gly Lys Trp Glu Gly Glu Leu Gly
 65 70 75 80
 Thr Asp Leu Val Ser Ile Pro His Gly Pro Asn Val Thr Val Arg Ala
 85 90 95
 Asn Ile Ala Ala Ile Thr Glu Ser Asp Lys Phe Phe Ile Asn Gly Ser
 100 105 110
 Asn Trp Glu Gly Ile Leu Gly Leu Ala Tyr Ala Glu Ile Ala Arg Pro
 115 120 125
 Asp Asp Ser Leu Glu Pro Phe Phe Asp Ser Leu Val Lys Gln Thr His
 130 135 140
 Val Pro Asn Leu Phe Ser Leu Gln Leu Cys Gly Ala Gly Phe Pro Leu
 145 150 155 160

Asn Gln Ser Glu Val Leu Ala Ser Val Gly Gly Ser Met Ile Ile Gly
 165 170 175
 Gly Ile Asp His Ser Leu Tyr Thr Gly Ser Leu Trp Tyr Thr Pro Ile
 180 185 190
 Arg Arg Glu Trp Tyr Tyr Glu Val Ile Ile Val Arg Val Glu Ile Asn
 195 200 205
 Gly Gln Asp Leu Lys Met Asp Cys Lys Glu Tyr Asn Tyr Asp Lys Ser
 210 215 220
 Ile Val Asp Ser Gly Thr Thr Asn Leu Arg Leu Pro Lys Lys Val Phe
 225 230 235 240
 Glu Ala Ala Val Lys Ser Ile Lys Ala Ala Ser Ser Thr Glu Lys Phe
 245 250 255
 Pro Asp Gly Phe Trp Leu Gly Glu Gln Leu Val Cys Trp Gln Ala Gly
 260 265 270
 Thr Thr Pro Trp Asn Ile Phe Pro Val Ile Ser Leu Tyr Leu Met Gly
 275 280 285
 Glu Val Thr Asn Gln Ser Phe Arg Ile Thr Ile Leu Pro Gln Gln Tyr
 290 295 300
 Leu Arg Pro Val Glu Asp Val Ala Thr Ser Gln Asp Asp Cys Tyr Lys
 305 310 315 320
 Phe Ala Ile Ser Gln Ser Ser Thr Gly Thr Val Met Gly Ala Val Ile
 325 330 335
 Met Glu Gly Phe Tyr Val Val Phe Asp Arg Ala Arg Lys Arg Ile Gly
 340 345 350
 Phe Ala Val Ser Ala Cys His Val His
 355 360

<210> 76
 <211> 63
 <212> DNA
 <213> Homo sapiens

<220>
 <221> misc_feature
 <222> (1)...(63)
 <223> n = A,T,C or G

<400> 76
 garacngayg argarcnga rgarccnggn mgnmngngnw snttygtnga ratggtn gay
 aay

60
 63

<210> 77
 <211> 21
 <212> PRT
 <213> Homo sapiens

<400> 77
 Glu Thr Asp Glu Glu Pro Glu Glu Pro Gly Arg Arg Gly Ser Phe Val
 1 5 10 15
 Glu Met Val Asp Asn
 20

<210> 78
 <211> 7
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Peptide inhibitor P3-P4' XD-V

<220>

<221> MOD_RES
<222> 3
<223> Xaa is hydroxyethylene or statine

<400> 78
Val Met Xaa Val Ala Glu Phe
1 5

<210> 79
<211> 11
<212> PRT
<213> Homo sapiens

<400> 79
Pro Glu Glu Pro Gly Arg Arg Gly Ser Phe Val
1 5 10

<210> 80
<211> 419
<212> DNA
<213> Artificial Sequence

<220>
<223> nucleotide insert in vector pCF

<400> 80
ctgtttgggct cgcggttgag gacaaactct tcgcggtctt tccagtactc ttggatcgga 60
aaccgcgtcgg cctccgaacg gtactccgcc accgagggac ctgagcgagt ccgcatcgac 120
cggatcggaa aacctctcga ctgttggggg gagtactccc tctcaaaagc gggcatgact 180
tctgcgctaa gattgtcagt ttccaaaaac gaggaggatt tgatattcac ctggcccgcg 240
gtgatgcctt tgagggtggc cgcgtccatc tggtcagaaa agacaatctt tttgttgtca 300
agcttgaggt gtggcaggct tgagatctgg ccatacaatt gaggacaat gacatccact 360
ttgcctttct ctccacaggt gtccactccc aggtccaact gcaggtcgac tctagaccc 419

<210> 81
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> Peptide inhibitor P4-P4' XD-V

<220>
<221> MOD_RES
<222> 4
<223> Xaa is hydroxyethylene or statine

<400> 81
Glu Val Met Xaa Val Ala Glu Phe
1 5

<210> 82
<211> 9
<212> PRT
<213> Homo sapiens

<220>
<223> APP fragment P5-P4' wt

<400> 82

Ser Glu Val Lys Met Asp Ala Glu Phe
1 5

<210> 83
<211> 9
<212> PRT
<213> Homo sapiens

<220>
<223> APP fragment P5-P4'wt

<400> 83
Ser Glu Val Asn Leu Asp Ala Glu Phe
1 5

<210> 84
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> APP fragment

<400> 84
Ser Glu Val Lys Leu Asp Ala Glu Phe
1 5

<210> 85
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> APP fragment

<400> 85
Ser Glu Val Lys Phe Asp Ala Glu Phe
1 5

<210> 86
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> APP fragment

<400> 86
Ser Glu Val Asn Phe Asp Ala Glu Phe
1 5

<210> 87
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> APP fragment

<400> 87

Ser Glu Val Lys Met Ala Ala Glu Phe
1 5

<210> 88
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> APP fragment

<400> 88
Ser Glu Val Asn Leu Ala Ala Glu Phe
1 5

<210> 89
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> APP fragment

<400> 89
Ser Glu Val Lys Leu Ala Ala Glu Phe
1 5

<210> 90
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> APP fragment

<400> 90
Ser Glu Val Lys Met Leu Ala Glu Phe
1 5

<210> 91
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> APP fragment

<400> 91
Ser Glu Val Asn Leu Leu Ala Glu Phe
1 5

<210> 92
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> APP fragment

<400> 92
Ser Glu Val Lys Leu Leu Ala Glu Phe

1 5

<210> 93
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> APP fragment

<400> 93
Ser Glu Val Lys Phe Ala Ala Glu Phe
1 5

<210> 94
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> APP fragment

<400> 94
Ser Glu Val Asn Phe Ala Ala Glu Phe
1 5

<210> 95
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> APP fragment

<400> 95
Ser Glu Val Lys Phe Leu Ala Glu Phe
1 5

<210> 96
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> APP fragment

<400> 96
Ser Glu Val Asn Phe Leu Ala Glu Phe
1 5

<210> 97
<211> 14
<212> PRT
<213> Artificial Sequence

<220>
<223> APP-derived fragment P10-P4' (D-V)

<400> 97
Lys Thr Glu Glu Ile Ser Glu Val Asn Leu Val Ala Glu Phe
1 5 10

<210> 98
<211> 35
<212> DNA
<213> Homo sapiens

<400> 98
cccgaagagc ccggccggag gggcagcttt gtcga

35

<210> 99
<211> 11
<212> PRT
<213> Homo sapiens

<400> 99
Glu Thr Asp Glu Glu Pro Glu Glu Pro Gly Arg
1 5 10

<210> 100
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<223> Recombinant 293T cells

<400> 100
Thr Gln His Gly Ile Arg Leu Pro Leu Arg
1 5 10

<210> 101
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Recombinant 293T cells

<400> 101
Met Val Asp Asn Leu Arg Gly Lys Ser
1 5

<210> 102
<211> 10
<212> PRT
<213> Artificial Sequence

<220>
<223> Recombinant CosA2 cells

<400> 102
Gly Ser Phe Val Glu Met Val Asp Asn Leu
1 5 10

<210> 103
<211> 4
<212> PRT
<213> Artificial Sequence

<220>
<223> APP substrate fragment:WT Sequence

<400> 103
Val Lys Met Asp
1

<210> 104
<211> 4
<212> PRT
<213> Artificial Sequence

<220>
<223> APP substrate fragment:Swedish Sequence

<400> 104
Val Asn Leu Asp
1

AS

Handwritten scribble or signature.